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NEW JERSEY COLLEGE OF MEDICINE

Jersey City, N.J.

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From - The Division of Hepatic Metabolism and Nutrition

Period Covering - April 1, 1965 through September 30, 1965

Studies to develop a method to detect early evidence of radiation damage during the period between April 1, 1965 through September 30, 1965 provided the following data:

1. It was demonstrated that small doses of proton radiation given over a local area of the liver induce a general increase in DNA synthesis in mesenchymal cells; this occurs in the absence of any damage to liver cells, and under conditions of our studies represents the most sensitive morphologic index to radiation injury.
2. There is a quantitative relationship between the disappearance of colloidal carbon and microaggregated I¹³¹ albumin and the degree of mesenchymal cell proliferation; this may permit use of the phagocytic index to detect early radiation damage and follow its course.

Proton radiation in doses of 2,000 to 11,500 rads was given over the liver. A diameter of 15 mm of tissue in the right lobe of the liver was irradiated. Four hours prior to killing, 1 microcurie per gram weight of tritiated thymidine was given. DNA synthesis was evaluated by autoradiographic and radiochemical techniques. It was demonstrated that a generalized increase in DNA synthesis occurred in mesenchymal cells and involved the non-irradiated liver, kidney, spleen, and intestines. This finding was interpreted as indicating that local liver injury primarily evokes a mesenchymal cell proliferation and that quantification of the phagocytic function of the reticuloendothelial system might be the best method for detecting radiation injury.

Studies were undertaken to determine the relationship of mesenchymal cell proliferation to phagocytic activity. Liver injury was induced in male adult Sprague Dawley rats with oral carbon tetrachloride (0.2 ml per 100 gm). Disappearance rate of colloidal carbon, microaggregated I¹³¹

albumin and indocyanine green were evaluated in the splenectomized intact animal. Four hours before killing, 1 microcurie of tritiated thymidine was given intraperitoneally. A sequential increase in phagocytic capacity, which paralleled increased DNA synthesis, was demonstrated.

Future Plans

Identical studies are now planned in which localized liver injury will be induced by proton radiation and the phagocytic index evaluated and related to DNA synthesis patterns in mesenchymal cells. These investigations will be simultaneously extended to man by (1) determining the phagocytic index before and during receipt of radiation therapy; (2) serial observations will be made of the phagocytic index in conditions associated with generalized mesenchymal cell proliferation.